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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,824	11/07/2001	Fernand Labrie	P/1259-636	4181

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
05/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/052,824	LABRIE, FERNAND	
	Examiner	Art Unit	
	YONG S. CHONG	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 14-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 14-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 4/7/2008. Claim(s) 4-13 have been cancelled. Claim(s) 1-3, 14-28 are pending. Claim(s) 14 has been amended. Claim(s) 1-3, 14-28 are examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and repeated below for Applicant's convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3, and 14-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Labrie (5,362,720), and Labrie et al. (WO 96/26201), and Applicant's admission regarding the prior art in the specification at 2 lines 3-4, for the same reasons of record in the previous Office Action November 18, 2004.

Labrie (5,362,720) teaches that estrogens such as l7l-estradiol are well known to be used in estrogen therapy in menopausal women. However, estrogens are known to induce estrogen-dependent diseases such as breast cancer. Labrie also discloses that androgenic compounds or androgenic steroids are useful in methods of treating or preventing estrogen-dependent diseases such as breast cancer. See abstract, col.1 line 35-38, col.4 lines 45-48, col.10, and claims 1-30.

Labrie et al. (WO 96/26201) discloses that the particular SERM, EM-652 (the instant elected species) or its pharmaceutically acceptable salts such as EM-652.HCl, have anti-estrogen activities and are therefore useful in methods of treating estrogen sensitive or estrogen-dependent diseases such as breast cancer, which is known estrogen-induced effects. See abstract, page 1, page 6-8, 10, and 19-21, and claims 11-12.

Applicant's admission regarding the prior art in the specification at 2 lines 3-4 teaches that Hormone Replace Therapy (e.g., administration of estrogens) is known to be useful in treatment of menopausal symptoms.

The prior art does not expressly disclose the employment of the combination of an estrogen such as l7β-estradiol and the particular SERM, EM-652.HCl, or maybe further combining an androgenic compound in a method of reducing or eliminating the

incidence of menopausal symptoms.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ of the combination of an estrogen such as l7β-estradiol and the particular SERM, EM-652.HCl, or to further combine an androgenic compound in a method of reducing or eliminating the incidence of menopausal symptoms.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the combination of an estrogen such as l7β-estradiol and the particular SERM, EM-652.HCl, or to further combine an androgenic compound in a method of reducing or eliminating the incidence of menopausal symptoms, since estrogens such as l7β-estradiol is well known in the art to be used in estrogen therapy or Hormone Replace Therapy in menopausal women for reducing or eliminating the incidence of menopausal symptoms.

Moreover, l7β-estradiol in combination with androgenic compounds or androgenic steroids is known to be capable to inhibiting breast tumor or cancer growth, and are therefore useful in methods of treating estrogen-dependent diseases, e.g., breast cancer according to Labrie. Further, the particular SERM, EM-652.HCl, is known to be in methods of treating estrogen-dependent diseases. Therefore, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as l7β -estradiol and the particular SERM, EM-652.HCl, or further combining an androgenic compound would be useful in reducing or eliminating the incidence of menopausal symptoms, while reducing the risk of or treating estrogen-dependent diseases such as breast cancer induced by estrogens during estrogen therapy in

menopausal women for reducing or eliminating the incidence of menopausal symptoms, since each of components herein is known to be useful in the same treatment, i.e., treating estrogen-dependent diseases.

Thus the claimed invention as a whole is clearly prima facie obvious over the teachings of the prior art.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Labrie (5,362,720), and Labrie (5,780,460, PTO-892), and Labrie et al. (WO 96/26201), and Applicant's admission regarding the prior art in the specification at 2 lines 3-4 for the same reasons of record in the previous Office Action dated November 18, 2004.

Labrie (5,36),720) teaches that estrogens such as l7β-estradiol are well known to be used in estrogen therapy in menopausal women. However, estrogens are known to induce estrogen-dependent diseases such as breast cancer. Labrie also discloses that androgenic compounds or androgenic steroids are useful in methods of treating or preventing estrogen-dependent diseases such as breast cancer. See abstract, col.1 line 35-38, col.4 lines 45-48, col.10, and claims 1-30.

Labrie (5,780,460) discloses that sex steroid precursors such as DEHA alone or in combination with an estrogen are useful in method of reducing or eliminating the incidence of menopausal symptoms, e.g., vaginal atrophy and diminished libido, and also useful in methods of treating or preventing estrogen-dependent diseases such as breast cancer. See abstract, col. 1-2, col.3 lines 44-55, and claims 1-2.

Labrie et al. (WO 96/26201) discloses that the particular SERM, EM-652 (the

instant elected species) or its pharmaceutically acceptable salts such as EM-652.HCl, have anti-estrogen activities and are therefore useful in methods of treating estrogen sensitive or estrogen-dependent diseases such as breast cancer, which is known estrogen-induced effects. See abstract, page 1, page 6-8, 10, and 19-21, and claims 11-12.

Applicant's admission regarding the prior art in the specification at pg. 2 lines 3-4 teaches that Hormone Replace Therapy (e.g., administration of estrogens) is known to be useful in treatment of menopausal symptoms.

The prior art does not expressly disclose the employment of the combination of an estrogen such as l7β-estradiol and the particular SERM, EM-652.HCl, and DHEA in a method of reducing or eliminating the incidence of menopausal symptoms.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ of the combination of an estrogen such as l7β-estradiol and the particular SERM, EM-652.HCl, and DHEA in a method of reducing or eliminating the incidence of menopausal symptoms.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the combination of an estrogen such as l7β-estradiol and the particular SERM, EM-652.HCl, and DHEA in a method of reducing or eliminating the incidence of menopausal symptoms, since estrogens such as l7β-estradiol are well known in the art to be used in estrogen therapy or Hormone Replace Therapy in menopausal women for reducing or eliminating the incidence of menopausal symptoms. Moreover, sex steroid precursors such as DEHA alone or in combination

with an estrogen (e.g., l7β-estradiol) is known to be useful in method of reducing or eliminating the incidence of menopausal symptoms, and also useful in methods of treating or preventing estrogen-dependent diseases such as breast cancer according to Labrie. Androgenic compounds are also known to be useful in methods of treating estrogen-dependent diseases. Further, the particular SERM, EM-652.HCI, is known to be in methods of treating estrogen-dependent diseases.

Therefore, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as l7β-estradiol and the particular SERM, EM-652.HCI, and DHEA, or further combining an androgenic compound would be useful in reducing or eliminating the incidence of menopausal symptoms, while reducing the risk of or treating estrogen-dependent diseases such as breast cancer induced by estrogens during estrogen therapy in menopausal women for reducing or eliminating the incidence of menopausal symptoms, since each of components herein is known to be useful in the same treatment, i.e., treating estrogen-dependent diseases.

Thus the claimed invention as a whole is clearly prima facie obvious over the teachings of the prior art.

Response to Arguments

Applicant argues that it is improper to use Kerkhoven case law to the obviousness rejection since breast cancer and menopause are entirely different conditions with different etiologies.

At the outset, it remains important to understand the entire scope of the cited prior art references. Labrie (US Patent 5,362,720) clearly state that while estrogens are well known to be used for estrogen therapy in menopausal women, an important side effect is the increased risk of estrogen-dependent diseases, such as breast cancer. Therefore, one of ordinary skill in the art knows that androgenic compounds or steroids are useful for balancing the side effects of estrogen administration by treating or preventing breast cancer.

Labrie (WO 96/26201) discloses the instantly elected species, EM-652, as the SERM compound, useful for treating estrogen-dependent diseases, such as breast cancer. Thus, Labrie teaches administration of EM-952 to treat breast cancer, whose onset or progress is aided by activation of the estrogen receptor (pg. 5) or caused or enhanced by estrogen activity (pg. 9).

Therefore, EM-652, was used in the obviousness rejection because of the need to balance the side effects (risk of breast cancer) due to the administration of estrogen, which is a completely different purpose than treating menopausal symptoms. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating menopausal symptoms without the increased risk of breast cancer by administering a combination of estrogen and EM-652.

Nonetheless, it is clear that l7β-estradiol in combination with androgenic compounds or androgenic steroids, particular SERM, EM-652.HCl, is known to be capable of treating estrogen-dependent diseases, which supports the argument made for the use of Kerkhoven case law in the obviousness rejection.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC

/SREENI PADMANABHAN/
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